REMARKS

I. Claim Status

Claims 1-26 are presently pending. Claims 1-6, 18-19, and 22-23 have been amended to define the claimed invention with greater particularity, and new claims 72 through 80 have been added to more particularly define specific embodiments of the claimed invention. Support for the amendments can be found in the Specification at, e.g., page 6, lines 29-31, page 7, lines 3-5, page 9, line 30, and page 24, lines 2-6 (amended claim 1) and in the originally filed claims (amended claims 3-6, 18-19, and 21-22). The amendment to claim 2 is inherent from original claim 2, and is being made at the request of the Examiner. Support for the new claims can be found in the Specification at, e.g., page 25, lines 13-14, page 33, lines 7-8, page 33, lines 7-8, and Example 1 at page 39, line 33 to page 40, line 1 (new claims 72 and 73); page 5, line 18 (new claims 74 and 75); page 33, line 27 (new claim 76); page 6, lines 5-8, page 27, lines 20-26 and page 36, lines 19-28 (new claim 77); page 17, line 18 (new claim 78); and original claims 22 and 23 (new claims 79 and 80). The specification has been amended to delete a sentence fragment. It is respectfully submitted that no new matter is introduced by entry of the subject amendments as the amendments and new claims are fully supported by the specification and original claims.

II. Information Disclosure Statement Received by the U.S.P.T.O. August 9, 2000

In the Office Action mailed December 4, 2001, the Examiner requested that Applicant provide copies of references cited in the Information Disclosure Statement received August 9, 2000 by the U.S. Patent and Trademark Office. In a telephone interview today, the Examiner indicated that he had located what he believed were the missing references submitted with the Information Disclosure Statement in question. Applicant's attorney expresses her appreciation to the Examiner for his search. Copies of any cited references not located will be furnished upon request.

III. Objection to the Claims and Indication of Allowable Subject Matter

Claims 18-26 have been objected to as being dependent on rejected claims. Applicant thanks the Examiner for the indication of allowable subject matter in claims 18-26. Pursuant to the Examiner's suggestion, claim 18 has been rewritten to include all of the limitations of the claims it depends from. Claims 19, 22, and 23 have been amended to specify their dependency on claim 18. In view of the amendments introduced herein, and the remarks below, Applicant respectfully requests the allowance of claims 18-26.

IV. The Rejections

1. 35 U.S.C. § 112, Second paragraph

Claims 1-7 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The rejections are respectfully traversed.

A. The Office Action alleges that the phrase, "an off-line parallel adjustment of cell growing conditions," and the term "parallel" are not clear. Claim 1 has been amended to specify an "off-line parallel purification system" to clarify that the "purifying" referred to is conducted in an off-line parallel purification system. Support for this amendment can be found at page 7, lines 3-5. The Specification describes the "parallel off-line purification system" at, for example, page 7, lines 3-33, page 39, line 33 to page 40, line 1, page 25, lines 13-14, page 33, lines 7-8, page 33, lines 7-8. More specifically, the off-line parallel purification system "is not coupled to a column separation system that functions in line with and sequential to the mass spectrometer." Specification at page 7, lines 12-13. To illustrate the distinction between parallel and non-parallel purification, the application provides liquid chromatography as an example of sequential, on-line purification. Specification at page 1, lines 32-33. Therefore, it

is believed that the term "off-line parallel purification system" is sufficiently described in the application.

B. The Examiner requests clarification as to whether column separation is to be excluded entirely from the method or if it is not excluded between steps (ii) and (iii). With regards to the purification system, the specification states that "[t]he system allows for off-line parallel purification of the products and/or reactants with no time-consuming column separation." Specification at page 24, lines 5-6. Therefore, the off-line parallel purification system does not involve column separation. To expedite prosecution and provide further clarity, claim 1 has been amended to include the step of "injecting the sample containing one or more non-column-separated component into a mass spectrometer, wherein the non-column-separated component has not undergone prior separation on a chromatography column." Support for this amendment can be found at page 6, lines 29-31.

C. The Office Action alleges that in claim 1, the phrase "performing flow-injection analysis using electrospray tandem mass spectrometry" is unclear. Applicant respectfully wishes to direct the Examiner to the Specification at page 43, lines 14-27 which provides clarity to the phrase in question.

D. The Office Action requests clarification of the term "component." Applicant respectfully submits that the term "component" is defined in the Specification, for example, at page 5, lines 2-11.

E. The Office Action also requests clarification as to whether in claim 2, the simultaneous execution of steps (i) and (ii) requires that the cells be alive and growing. Claim 2 has been amended to clarify that the one or more cell is alive during step (ii).

F. Claims 3-7 have been rejected for an alleged omission of essential steps relating to a functional assay for determining the activity of a component or a means of relating a detected product with an activity. Claims 3-6 have been amended to delete the term "activity." This amendment is incorporated into claim 7 by its dependency on claim 5. Applicant respectfully submits that, in view of the amendment, further steps relating to activity detection are not required.

G. Claims 5 and 6 have been rejected as being indefinite for specifying both a broad range and a narrow range. Claims 5 and 6 have been amended to each recite a single range.

In view of the amendments and remarks above, Applicant respectfully requests withdrawal of the rejection of claims 1-7 under 35 U.S.C. § 112, second paragraph.

2. 35 U.S.C. § 102

Claims 1 and 12-17 stand rejected under 35 U.S.C. 102(e) as being allegedly anticipated by U.S. Patent No. 6,258,605 (Chace). This rejection is respectfully traversed.

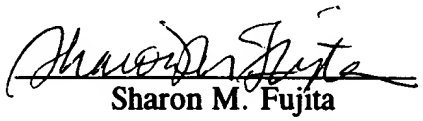
The Chace patent, which describes the use of blood spotted on filter paper in a screen, fails to describe growing one or more cell in vitro as is required in step (i) of amended claim 1. Therefore, the Chace patent does not anticipate the invention as claimed. Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 1 and 12-17 under 35 U.S.C. § 102(e).

CONCLUSION

In light of the foregoing amendments and remarks, it is believed that the application is in condition for allowance. Accordingly, reconsideration and favorable action on all claims is earnestly solicited. If there are any questions concerning this communication, the Examiner is invited to call the undersigned at the telephone number provided below so that prompt disposition of this application can be achieved.

Respectfully submitted,

June 4, 2002

By: 
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APPENDIX A

MARKED UP CLAIMS ILLUSTRATING AMENDMENTS

1. (AMENDED) A method of performing high throughput mass spectrometry screening, the method comprising:

(i) growing one or more cell in vitro;

(ii) purifying a sample containing one or more non-column-separated component from the one or more cell, the purifying comprising an off-line parallel [adjustment of cell growing conditions] purification system;

(iii) injecting the sample containing one or more non-column-separated component into a mass spectrometer, wherein the non-column-separated component has not undergone prior separation on a chromatography column; and,

[(iii)] (vi) performing flow-injection analysis using electrospray tandem mass spectrometry on the one or more non-column-separated component from the one or more cell, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening of the one or more non-column-separated component.

2. (AMENDED) The method of claim 1, wherein step (i) occurs simultaneously with step (ii), and wherein said one or more cell is alive during step (ii).

3. (AMENDED) The method of claims 1 or 2, wherein at least about 100 cell colonies are screened for presence [or activity] of the one or more non-column-separated component in less than an hour.

4. (AMENDED) The method of claim 1, wherein at least about 200 cell colonies are screened for presence [or activity] of the one or more non-column-separated component in less than an hour.

5. (AMENDED) The method of claim 1, wherein at least about 500 cell colonies[, at least about 1000 cell colonies, at least about 5000 cell colonies, at least about 10,000 cell colonies, at least about 25,000 cell colonies, or at least about 100,000 cell colonies] are screened for presence [or activity] of the one or more non-column-separated component in less than an hour.

6. (AMENDED) The method of claim 1, wherein [at least about 200 cell colonies,] at least about 1000 cell colonies[, at least about 25,000 cell colonies, at least about 100,000 cell colonies, or at least about 500,000 cell colonies or more] are screened for the presence [or activity] of the one or more non-column-separated component in about 1 day.

18. (AMENDED) A method of performing high throughput mass spectrometry screening, the method comprising:

(i) growing one or more cell in vitro;

(ii) purifying a sample containing one or more non-column-separated component from the one or more cell,

wherein the purifying comprises attaching the one or more non-column separated component to a solid support in an off-line parallel purification system, and

[The method of claim 17,] wherein the solid support comprises one or more magnetic beads, one or more agarose beads, one or more polystyrene beads, one or more pins, a microwell plate, or a membrane;

(iii) injecting the sample containing the one or more non-column-separated component into a mass spectrometer, wherein the non-column-separated component has not undergone prior separation on a chromatography column; and,

(iv) performing flow-injection analysis using electrospray tandem mass spectrometry on the one or more non-column-separated component from the one or more cell, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening of the one or more non-column-separated component.

19. (AMENDED) The method of claim [17] 18, wherein the one or more non-separated column component comprises a library of enzymes, which enzymes each comprises a tag moiety, and wherein the solid support comprises a tag binding moiety.

22. (AMENDED) The method of claim [1] 18, wherein the one or more non-column-separated component comprises one or more enzyme substrate and one or more product of an enzymatic reaction, the method further comprising simultaneously quantifying the amount of the one or more product of an enzyme reaction and the one or more enzyme substrate.

23. (AMENDED) The method of claim [1] 18, wherein performing flow injection analysis using electrospray tandem mass spectrometry comprises performing [or more] a method selected from the group consisting of[:] neutral loss mass spectrometry and parent ion mass spectrometry.

APPENDIX B

MARKED UP PARAGRAPHS ILLUSTRATING AMENDMENTS MADE TO SPECIFICATION

Please delete the paragraph beginning at page 4, line 20 and ending at page 4, line 31, and substitute therefore the following paragraph:

In another embodiment, the present invention provides a method for monitoring products or reactants, such as in enzyme reactions, by high throughput mass spectrometry by providing a cell or bacteria that has been transformed with a plasmid containing one or more member of a library, e.g., of related gene sequences, such as related enzyme gene sequences. One or more cells or a cell colony or culture is grown from the cell; producing one or more product or reactant from the cell colony or culture in a biological matrix, thereby producing a non-column-separated sample; purifying the non-column separated sample from the biological matrix using an off-line parallel adjustment of the biological matrix, and monitoring the non-column separated sample by flow-injection analysis using electrospray tandem mass spectrometry, thereby monitoring the one or more product or reactant. In this way, enzyme reactions and their products can be studied at high throughput levels. [Alternative libraries are also]